

TTGCTGATTTCCTCGAAGACTACATCGATTTTGCGATAAATGAGCCAGATCTACTTCGTC
1261 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 1320
A D F L E D Y I D F A I N E P D L L R P
90 100
CAGTAGTGATTGCTCCACAATTTTCCCGACAAATGCTCGATAGGAACTATTGCTTGGGA
1321 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1380
V V I A P Q F S R Q M L D R K L L L G N
110 120
T n2274
↑
ATGTTCCAAAACAAATGACATGCTATATTTCGAGAGTATCACGTGGATCGAGTGATCAAAA
1381 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1440
V P K Q M T C Y I R E Y H V D R V I K K
130 140
AGCTCGACGAGATGTGTGATTAGGTGAGAAAACCTGGAAGCTCTCGTGTTTATTATAATC
1441 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1500
L D E M C D L D
150
TTGCTTAAACTTCAGACTCCTTTTTTCTGTTTCTACACGGCCGAGCTGGATCCGAAAAT
1501 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1560
S F F L F L H G R A G S G K S
160
CAGTAATTGCATCACAAGCTCTTTCGAAATCTGACCAACTTATTGGAATGTGAGTGGTAT
1561 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1620
V I A S Q A L S K S D Q L I G I
170 180
TATCTGAATCTACGGATCTTCATTCTATTACAGAAATTATGATTCAATCGTTTGGCTCAA
1621 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1680
N Y D S I V W L K
190
AGATAGTGGAACAGCTCCAAAATCTACATTTCGATTTATTTACGGATATTTTGCTGATGCT
1681 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1740
D S G T A P K S T F D L F T D I L L M L
200 210
A n1920/n2247
↑ Intron 3
AAAGTGAGTGAATAGAGTGCATGTAACATTCAGCATGATTTTGAAATTATGAAAATTTGA
1741 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1800
K
CCTGGTTAGCTTTTAAATTTGATATTTCTGTGACGCTTGCATGTTTTGTGTGTTTGAAGACG
1801 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1860
AGCCCGTGTTGTGAGCGACACGGATGACTCGCATTCGATCACCGACTTCATTAACCGTGT
1861 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1920
A n2273
↑
TCTTTCAAGAAGCGAAGACGATCTTCTCAATTTCCCATCGGTGGAGCATGTCACGTCAGT
1921 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1980
S E D D L L N F P S V E H V T S V
220

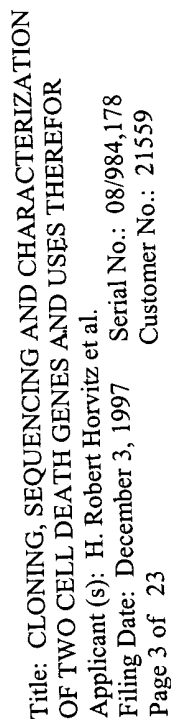


FIG. 1C

1981 TGTACTCAAAAGGATGTAAGTTGCTTGCCGATTCTGGTACAATATCTTAAATTATTGGT 2040
-----+-----+-----+-----+-----+-----+-----+-----+-----+
V L K R M

230
TTT TAGATCTGCAACGCACTCATTGATCGTCCAAATAC TTTATTTCGTATTGATGACGTA
2041 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2100
I C N A L I D R P N T L F V F D D V
240 250

A n1948 T n1947
↑ ↑
GTTCAAGAAGAAA CAATTCGTTGGGCTCAGGAGCTACGTCTTCGATGTCTTGTA ACTACT
2101 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2160
V Q E E T I R W A Q E L R L R C L V T T
260 270
CGTGACGTGGAAATATCAAATGCTGCTTCTCAAACATGCGAATTCATTGAAGTGACATCA
2161 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2220
R D V E I S N A A S Q T C E F I E V T S
280 290
TTGGAATCGATGAATGTTATGATTTTCTAGAAGCTTATGGAATGCCGATGCCTGTTGGA
2221 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2280
L E I D E C Y D F L E A Y G M P M P V G
300 310
Tc4 n1416
↓
GAAAAAGAAGAAGATGTGCTTAATAAAACAATCGAACTAAGCAGTGGAATCCAGCAACG
2281 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2340
E K E E D V L N K T I E L S S G N P A T
320 330

Intron 5
CTTATGATGTTTTTCAAGTCTTGTGAACCGAAAAACATTTGAAAAGT GAGTGGGACATACC
2341 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2400
L M M F F K S C E P K T F E K
330
AATTTGAGACTTTTTAAATAATTTATTCTACAATAAAAGTTAATCAAAAAGTTTCATAGC
2401 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2460
TGATTGTCTTTAAATTTTACGAATTGAGGATCAAAATCAAGAATTAGGATCCTGGCACGA
2461 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2520
GAGAAAACTGTGTAGCTACCGTACCCGAGAGATTTTCTTGATATTTGCCATCGATTTAAT
2520 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2580
TTTTTAAGAAAATTATCGTTTTTACATAATTGAACAAGAGATACACGGTCTCGACCCGACG
2581 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2640
GAAATTTTTTAAATGAAAGCGAGTATGAGCCTGTTTTTCATTATTTTCGATTTTCTCTTG
2641 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2700
TTGTTTCTTTTTATTTAAAGCCTTTTTATTTTGAACAAGTCTAAAAATATTA AAAA CTGA
2701 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2760
ATAAAATATTTAAAAAAAATCAAGTAAATAGAAAAACAGCAAGGCTGGAGACTACTGTA
2760 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2820
CTTCTTAAATCCGCATACTCTTTTTATTTAATCATTTTCCGGAATGTCGAAACGAAATAA
2821 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2880
TACATTTTTTAGTCCAAAATCGCTAGGTATATTCTTAAAATTATCAAAACATTTTGCATTCA



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FIG. 1D

2881 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2940
GAATGGCACAGCTTAATAACAAATTGGAAAGTCGAGGATTAGTCGGTGTGAATGTATCA
2941 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3000
M A Q L N N K L E S R G L V G V E C I T
340 350

3001 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3060
CCCCTTACTCGTACAAGTCACTCGCAATGGCTCTTCAAAGATGTGTTGAAGTTTGTGTCAG
P Y S Y K S L A M A L Q R C V E V L S D
360 370

3061 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3120
ATGAGGATCGAAGTGCTCTTGCTTTTCGCAGTTGTGATGCCTCCTGGAGTTGATATACCCG
E D R S A L A F A V V M P P G V D I P V
380 390
A n1894
↑

3121 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3180
TCAAGCTATGGTCATGTGTTATTCCAGTTGATATTTGTTCAAATGAAGAAGAACAATTGG
K L W S C V I P V D I C S N E E E Q L D
400 410

3181 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3240
ATGATGAAGTTGCGGATCGGTTGAAAAGACTCAGCAAGTATGAGTCTTGAAATTTGAAGA
D E V A D R L K R L S K
420
Intron 6

3241 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3300
TTTAAATTAACACTTAAAATTTTCAGACGTGGAGCTCTTCTCAGTGGAAAACGAATGCCCCG
R G A L L S G K R M P V
430 440

3301 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3360
TTTTGACATTCAAATTGATCATATTATCCATATGTTCTTGAAACACGTCGTTGATGCAC
L T F K I D H I I H M F L K H V V D A Q
450 460

3361 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3420
AAACTATCGCGTATGCTGAAAATGTCTCAACTTTCAATTAAATTTTAAATTTTCAGAAAT
T I A N
GGAATCTCAATTCTCGAGCAGCGTCTTCTTGAAATAGGAAACAATAATGTATCAGTACCG
3421 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3480
G I S I L E Q R L L E I G N N N V S V P
470 480

3481 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3540
GAGCGACATATACCATCACATTTCCAAAAATTCGTCGTTTCATCAGCCAGTGAGATGTAT
E R H I P S H F Q K F R R S S A S E M Y
500 510

3541 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3600
CCAAAACTACAGAAGAACTGTGATCCGTCCTGAAGACTTCCCAAAGTTCATGCAATTG
P K T T E E T V I R P E D F P K F M Q L
520 530

3601 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3660
CACCAGAAATTTCTATGACTCCCTCAAAAATTTTGCATGCTGTTAAAACCTATCGTGTACA
H Q K F Y D S L K N F A C C *
540

ATATTGCCTGTATATTCCCCTCGAAATACGTTTATACTTTTTTCGCACGAGTTTTCTCATT



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FIG. 1E

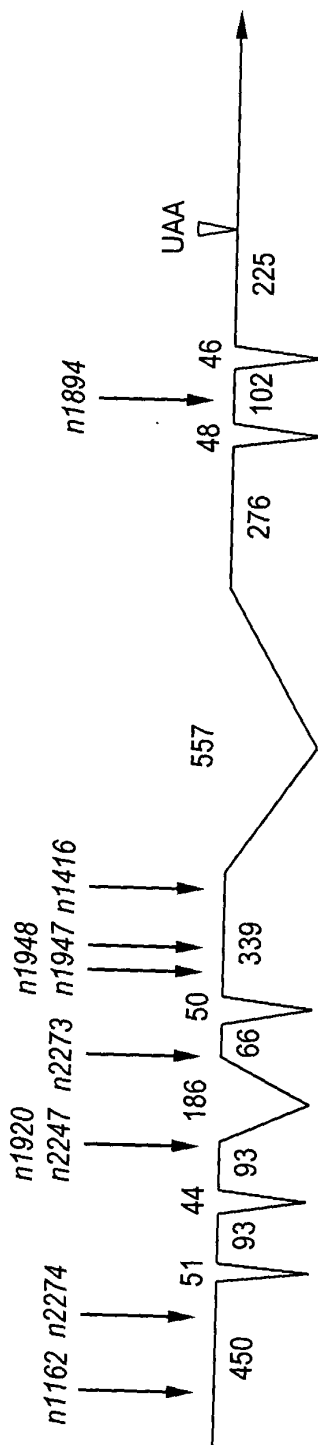
3661 -----+-----+-----+-----+-----+-----+-----+ 3720
TTTTCAATTTGTAATGTTTTATTTCTCTCCAAAATTTTCAGATCTATCCCAAATGTTCTTA
3721 -----+-----+-----+-----+-----+-----+-----+ 3780
AATTTAATGTTTTCTACAGATACTCAACACATCTTGTTTCATCTCATCCTTGCTTTTTTTT
3781 -----+-----+-----+-----+-----+-----+-----+ 3840
TTTCAAATATATTCAAGTTCTTTTATAATTTTAATTAATCGAATTAATACATTCACGTAA
3841 -----+-----+-----+-----+-----+-----+-----+ 3900
AGAATTTTCGTGGACTATTATTTTATCGCATCCAAATGATTTATTCCCTATTGTTGAAAC
3901 -----+-----+-----+-----+-----+-----+-----+ 3960
TTCCAAATTGATCATTTTTTAAACACGCCTCATTAAATTGAAAGTCGTACTTTTAGTCTCG
3961 -----+-----+-----+-----+-----+-----+-----+ 4020
AACATGAAGTAAGTTATTTTCTGTGTTCTAAATTCAAAGTGCATTCCAAAAGGACATTTG
4021 -----+-----+-----+-----+-----+-----+-----+ 4080
ATGAGTTTTTCACGAAAACCGTAATTTTACAATTTCTTTTCAGTTTTGAAGATGTTTCGAT
4081 -----+-----+-----+-----+-----+-----+-----+ 4140
TTCTTTCTCTGTTGGCGTCATTACTACATTTGCTTTGCTGCTTCACTTTATCGAGATTC
4141 -----+-----+-----+-----+-----+-----+-----+ 4200
TTGCCATCAATGGAGTTCCATCTAGACCGATAGCAGTCTTCATATCATTATCCCTGTATA
4201 -----+-----+-----+-----+-----+-----+-----+ 4260
TTGTAATGTTTCAGTATTTTAACTTATCGATTACGTACTATATTTCAGTGGTTCACTGTTT
4261 -----+-----+-----+-----+-----+-----+-----+ 4320
TCGGTCAATGGGTGACACGTGCTCGACGANNNAATTTTCAACGAACGCAATCTCCTAGTCA
4320 -----+-----+-----+-----+-----+-----+-----+ 4380
CTTATCAACCAAGAGCCCTCACCCATG
4380 -----+-----+-----+-----+-----+-----+-----+ 4407

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997
Page 5 of 23
Serial No.: 08/984,178
Customer No.: 21559

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Title: CLONING, SEQUENCING AND CHARACTERIZATION
 OF TWO CELL DEATH GENES AND USES THEREFOR
 Applicant (s): H. Robert Horvitz et al.
 Filing Date: December 3, 1997 Serial No.: 08/984,178
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FIG. 2





Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR

Applicant (s): H. Robert Horvitz et al.

Filing Date: December 3, 1997 Serial No.: 08/984,178

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FIG. 3

	10	12	14	18	21
	X	Y	Z	-X	-Z
	D	N	S	T	E
Calcium-binding loop consensus		D	N	S	
			D	E	
				Q	
				D	
				N	
EF-hand consensus	O * O * O G * * O * * E				
ced-4 sequence 1	<u>Y</u> N N Q S <u>H</u> L A D F L E				
sequence 2	<u>S</u> L <u>E</u> I D <u>E</u> C Y D F L E				
Parvalbumin (carp)	D Q D K S G F I <u>E</u> E D E				
(hake)	D Q D K D <u>D</u> F I <u>G</u> E D E				
(ray)	D S D G D <u>H</u> K I <u>G</u> V D E				
SCBP (<i>Amphioxus I</i>)	D I N K D <u>D</u> V V S W E E				
ICaBP (bovine)	A K <u>E</u> G D <u>P</u> Q L S K E E				
	D K N G D <u>G</u> E V S F E E				
Troponin C (rabbit)	D A D G <u>G</u> G D I S V K E				
	D E D G <u>S</u> G T I D F E E				
	D R N A D G Y I D A E E				
	D K N N D G R I D F D E				
Calmodulin (bovine)	D K D G N G T I T T K E				
Trypsinogen	<u>L</u> G <u>E</u> D N <u>I</u> N V V E G N E				
Fibrinogen	D N D N D <u>K</u> F E G N C A E				
Villin	<u>G</u> V D P S <u>R</u> K E N H L S				
GBP	D L N K D G Q I Q <u>_</u> I E				

TAAATCGGCTCGACATTATCGTATTAAGGAATCACAAAATTCTGAGAATGCGTACTGCGC
 1321 -----+-----+-----+-----+-----+-----+ 1380

 AACATATTTGACGGCAAAATATCTCGTAGCGAAAACTACAGTAATTCTTTAAATGACTAC
 1381 -----+-----+-----+-----+-----+-----+ 1440



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FIG. 4B

Title: CLONING, SEQUENCING AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant (s): H. Robert Horvitz et al.
Filing Date: December 3, 1997
Page 9 of 23
Serial No.: 08/984,178
Customer No.: 21559

-----> Repeat 1
<-----
1441 TGTAGCGCTTGTGTCGATTTACGGGCTCAATTTTTGAAAATAATTTTTTTTCGAATTT 1500
-----+-----+-----+-----+-----+-----+-----+
1501 TGATAACCCGTAAATCGTCACAACGCTACAGTAGTCATTTAAAGGATTACTGTAGTTCTA 1560
-----+-----+-----+-----+-----+-----+-----+
1561 GCTACGAGATATTTTGC GCGCCAAATATGACTGTAATACGCATTCTCTGAATTTTGTGTT 1620
-----+-----+-----+-----+-----+-----+-----+
1621 TCCGTAATAATTTT CACAAGATTTTGGCATTCCACTTTAAAGGCGCACAGGATTTATCCCA 1680
-----+-----+-----+-----+-----+-----+-----+
1681 ATGGGTCTCGGCACGCAAAAAGTTTGATAGACTTTTAAATTCTCCTTGCAATTTTAAATTC 1740
-----+-----+-----+-----+-----+-----+-----+
1741 AATTACTAAAATTTTCTGTAATTTTCTGTTAAATTTTAAATCAGTTTTCTAATATT 1800
-----+-----+-----+-----+-----+-----+-----+
1801 TTCCAGGCTGACAAACAGAAACAAAAACACAACAAACATTTTAAAAATCAGTTTTCAAAT 1860
-----+-----+-----+-----+-----+-----+-----+
1861 TAAAAATAACGATTTCTCATTGAAAATTGTGTTTATGTTTGCGAAAAATAAAGAGAACT 1920
-----+-----+-----+-----+-----+-----+-----+
1921 GATTCAAAACAATTTTAACAAAAAAACCCAAAAATTCGCCAGAAATCAAGATAAAAAA 1980
-----+-----+-----+-----+-----+-----+-----+
1981 TTCAAGAGGGTCAAAATTTTCCGATTTTACTGACTTTCACCTTTTTTTTCGTAGTTTCAGT 2040
-----+-----+-----+-----+-----+-----+-----+
2041 GCAGTTGTTGGAGTTTTTGACGAAACTAGGAAAAAATCGATAAAAAATTACTCAAATCG 2100
-----+-----+-----+-----+-----+-----+-----+
2101 AGCTGAATTTTGAGGACAATGTTTAAAAAAAACACTATTTTCCAATAATTTCACTCAT 2160
-----+-----+-----+-----+-----+-----+-----+

2161 TTTTCAGACTAAATCGAAAATCAAATCGTACTCTGACTACGGGTCAGTAGAGAGGTCAACC 2220
-----+-----+-----+-----+-----+-----+-----+
2221 ATCAGCCGAAGATGATGCGTCAAGATAGAAGGAGCTTGCTAGAGAGGAACATTATGATGT 2280
-----+-----+-----+-----+-----+-----+-----+
M M R Q D R R S L L E R N I M M F
1 10
T (n1040)
|
2281 TCTCTAGTCATCTAAAAGTCGATGAAATTCTCGAAGTTCTCATCGCAAAACAAGTGTGTA 2340
-----+-----+-----+-----+-----+-----+-----+
S S H L K V D E I L E V L I A K Q V L N
20 30
| Intron 1
2341 ATAGTGATAATGGAGATATGATTAATGTGAGTTTTTAATCGAATAATAATTTTAAAAAAA 2400
-----+-----+-----+-----+-----+-----+-----+
S D N G D M I N
40



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FIG. 4C

AATTGATAATATAAAGAATATTTTTGCAGTCATGTGGAACGGTTCGCGAGAAGAGACGGG
2401 -----+-----+-----+-----+-----+-----+-----+ 2460
S C G T V R E K R R E
50

A (n718)

AGATCGTGAAAGCAGTGCAACGACGGGGAGATGTGGCGTTCGACGCGTTTTATGATGCTC
2461 -----+-----+-----+-----+-----+-----+-----+ 2520
I V K A V Q R R G D V A F D A F Y D A L
60 70

Intron 2

TTCGCTCTACGGGACACGAAGGACTTGCTGAAGTTCTTGAACCTCTCGCCAGATCGTAGG
2521 -----+-----+-----+-----+-----+-----+-----+ 2580
R S T G H E G L A E V L E P L A R S
80 90

TTTTTAAAGTTCGGCGCAAAGCAAGGGTCTCACGAAAAAAGAGGCGGATCGTAATTTT
2581 -----+-----+-----+-----+-----+-----+-----+ 2640
GCAACCCACCGGCACGGTTTTTCTCCGAAATCGGAAATTATGCACTTTCCCAAATAT
2641 -----+-----+-----+-----+-----+-----+-----+ 2700
TTGAAGTGAAATATATTTTATTTACTGAAAGCTCGAGTGATTATTTATTTTAACTA
2701 -----+-----+-----+-----+-----+-----+-----+ 2760
ATTTTCGTGGCGCAAAGGCCATTTTGTAGATTGCGGAAAATACTTGTCACACACACAC
2761 -----+-----+-----+-----+-----+-----+-----+ 2820

ACACACATCTCCTTCAAATATCCCTTTTTCCAGTGTGACTCGAATGCTGTGCAATTCTGA
2821 -----+-----+-----+-----+-----+-----+-----+ 2880
V D S N A V E F E
100

GTGTCCAATGTCACCGGCAAGCCATCGTCGGAGCCGCGCATTGAGCCCCGCCGGCTACAC
2881 -----+-----+-----+-----+-----+-----+-----+ 2940
C P M S P A S H R R S R A L S P A G Y T
110 120

TTCACCGACCCGAGTTCACCGTGACAGCGTCTCTTCAGTGTCTCATTCACCTTCTTATCA
2941 -----+-----+-----+-----+-----+-----+-----+ 3000
S P T R V H R D S V S S V S S F T S Y Q
130 140

GGATATCTACTCAAGAGCAAGATCTCGTTCTCGATCGCGTGCACCTTCATTCATCGGATCG
3001 -----+-----+-----+-----+-----+-----+-----+ 3060
D I Y S R A R S R S R S R A L H S S D R
150 160

Intron 3

ACACAATTATTCATCTCCTCCAGTCAACGCATTTCCAGCCAACCTTGTATGTTGATGCG
3061 -----+-----+-----+-----+-----+-----+-----+ 3120
H N Y S S P P V N A F P S Q P S
170



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FIG. 4D

Repeat 1

```
-----  
AACACTAAATTCTGAGAAATGCGCATTACTCAACATATTTGACGCGCAAATATCTCGTAGC  
3121 -----+-----+-----+-----+-----+-----+ 3180  
-----  
GAAAAATACAGTAACCCCTTTAAATGACTATTGTAGTGTGATTACGGGCTCGATTTTCG  
3181 -----+-----+-----+-----+-----+-----+ 3240  
-->  
AAACGAATATATGCTCGAATTGTGACAACGAATTTAATTTGTCATTTTGTGTTTTCTT  
3241 -----+-----+-----+-----+-----+-----+ 3300
```

Repeat 1

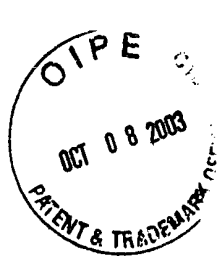
```
<-----  
TTGATATTTTTGATCAATTAATAAATTATTTCCGTAAACAGACACCAGCGCTACAGTACT  
3301 -----+-----+-----+-----+-----+-----+ 3360  
-----  
CTTTTAAAGAGTTACAGTAGTTTTTCGCTTCAAGATATTTTGAAAAGAATTTTAAACATTT  
3361 -----+-----+-----+-----+-----+-----+ 3420  
TGAAAAAAAAATCATCTAACATGTGCCAAAACGCTTTTTTCAAGTTTCGCAGATTTTTTGA  
3421 -----+-----+-----+-----+-----+-----+ 3480
```

Repeat 2

```
-----  
TTTTTTTTCATTCAAGATATGCTTATTAACACATATAATTATCATTAATGTGAATTTCTTG  
3481 -----+-----+-----+-----+-----+-----+ 3540  
-----  
TAGAAATTTTGGGCTTTTCGTTCTAGTATGCTCTACTTTTGAAATTGCTCAACGAAAAAA  
3541 -----+-----+-----+-----+-----+-----+ 3600  
-----  
TCATGTGGTTTGTTTCATATGAATGACGAAAAATAGCAATTTTTTATATATTTTCCCCTAT  
3601 -----+-----+-----+-----+-----+-----+ 3660  
-----  
TCATGTTGTGCAGAAAAATAGTAAAAAGCGCATGCATTTTTCGACATTTTTCATCGA  
3661 -----+-----+-----+-----+-----+-----+ 3720  
----->  
ACGACAGCTCACTTCACATGCTGAAGACGAGAGACGCGGAGAAATACCACACATCTTTCT  
3721 -----+-----+-----+-----+-----+-----+ 3780
```

Repeat 2

```
<-----  
GCGTCTCTCGTCTTCAGCATGTGAAATGGGATCTCGGTCGATGTAAAAAATGTCGAATA  
3781 -----+-----+-----+-----+-----+-----+ 3840  
-----  
ATGTAAAAAATGCATGCGTTTTTTTTTACACTTTTCTGCACAAATGAATAGGGGGAAAAATGT  
3841 -----+-----+-----+-----+-----+-----+ 3900
```



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FIG. 4E

ATTAAAATACATTTTTTGTATTTTTCAACATCACATGATTAACCCCATTTATTTTTTCGTT
3901 -----+-----+-----+-----+-----+ 3960

GAGCAACTTAAAAAGTAGAGAATATTAGAGCGAAAACCAAATTTCTTCAAGATATTACC
3961 -----+-----+-----+-----+-----+ 4020

TTTATTGATAATTATAGATGTTAATAAGCATATCTTGAATGAAAGTCAGCAAAAATATGT
4021 -----+-----+-----+-----+-----+ 4080

GCGAAACACCTGAAAAAATCAAAAATCTGCGAAAATTGAAAAATGCATTAAAAATACA
4081 -----+-----+-----+-----+-----+ 4140

TTTTTGCATTTTCTACATCACATGAATGTAGAAAATTAAAAGGGAAATCAAAATTTCTA
4141 -----+-----+-----+-----+-----+ 4200

GAGGATATAATTGAATGAAACATTGCGAAATTAAAATGTGCGAAACGTCAAAAAAGAGGA
4201 -----+-----+-----+-----+-----+ 4260

AATTTGGGTATCAAAATCGATCCTAAAACCAACACATTTTCAGCATCCGCCAACTCTTCAT
4261 -----+-----+-----+-----+-----+ 4320
S A N S S F
180

TCACCGGATGCTCTTCTCTCGGATACAGTTCAAGTCGTAATCGCTCATTTCAGCAAAGCTT
4321 -----+-----+-----+-----+-----+ 4380
T G C S S L G Y S S S R N R S F S K A S
190 200

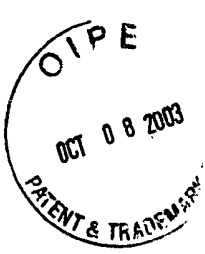
CTGGACCAACTCAATACATATTCCATGAAGAGGATATGAACTTTGTGCGATGCACCAACCA
4380 -----+-----+-----+-----+-----+ 4440
G P T Q Y I F H E E D M N F V D A P T I
210 220

TAAGCCGTGTTTTTCGACGAGAAAAACCATGTACAGAACTTCTCGAGTCCTCGTGGAATGT
4441 -----+-----+-----+-----+-----+ 4500
S R V F D E K T M Y R N F S S P R G M C
230 240

GCCTCATCATAAATAATGAACACTTTGAGCAGATGCCAACACGGAATGGTACCAAGGCCG
4501 -----+-----+-----+-----+-----+ 4560
L I I N N E H F E Q M P T R N G T K A D
250 260

ACAAGGACAATCTTACCAATTTGTTTCAGATGCATGGGCTATACGGTTATTTGCAAGGACA
4561 -----+-----+-----+-----+-----+ 4620
K D N L T N L F R C M G Y T V I C K D N
270 280

| Intron 4
ATCTGACGGGAAGGGTACGGCGAAATTATATTACCCAAACGCGAAATTTGCCATTTTGCG
4621 -----+-----+-----+-----+-----+ 4680
L T G R



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FIG. 4F

Repeat 3

----->
CCGAAAATGTGGCGCCCGTCTCGACACGACAATTTGTGTAAATGCAAAAATGTATAAT
4681 -----+-----+-----+-----+-----+-----+ 4740
TTTGCAAAAAACAAAATTTGAACTTCCGCGAAAATGATTTACCTAGTTTCGAAATTTTC
4741 -----+-----+-----+-----+-----+-----+ 4800
GTTTTTCCGGCTACATTATGTGTTTTTCTTAGTTTTTCTATAATATTTGATGTAAAAA
4801 -----+-----+-----+-----+-----+-----+ 4860
ACCGTTTGTAATTTTCAGACAATTTTCCGCATACAAAACCTTGATAGCACGAAATCAATT
4861 -----+-----+-----+-----+-----+-----+ 4920
TTCTGAATTTTCAAAATTATCCAAAAATGCACAATTTAAAATTTGTGAAAATTGGCAAAC
4921 -----+-----+-----+-----+-----+-----+ 4980
GGTGTTCATATGAAATGTATTTTAAAAACTTTAAAAACCACTCCGAAAAGCAATAA
4981 -----+-----+-----+-----+-----+-----+ 5040
AAATCAAAAACACGTCACAATTCAAATTCAAAAGTTATTCATCCGATTTGTTTATTTTTG
5041 -----+-----+-----+-----+-----+-----+ 5100
CAAAATTTGAAAAATCATGAAGGATTAGAAAAAGTTTATAACATTTTTTCTAGATTTT
5101 -----+-----+-----+-----+-----+-----+ 5160
TCAAAATTTTTTTTAAACAATCGAGAAAAAGAGAATGAAAAATCGATTTTAAAAATATCC
5161 -----+-----+-----+-----+-----+-----+ 5220

Repeat 3

<-----
ACAGCTTCGAGAGTTTGAAATTACAGTACTCCTTAAAGGCGCACACCCCATTTGCATTGG
5221 -----+-----+-----+-----+-----+-----+ 5280

ACCAAAAATTTGTCGTGTCGAGACCAGGTACCGTAGTTTTTGTGCGAAAAATTGCACCAT
5281 -----+-----+-----+-----+-----+-----+ 5340
TGGACAATAAACCTTCCTAATCACCAAAAAGTAAAATTGAAATCTTCGAAAAGCCAAAAA
5341 -----+-----+-----+-----+-----+-----+ 5400
ATTCAAAAAAAAAGTCGAATTTTCGATTTTTTTTTTTGGTTTTTGGTCCCAAAAACCAAAA
5401 -----+-----+-----+-----+-----+-----+ 5460
AAATCAATTTTCTGCAAAATACCAAAAAGAAACCCGAAAAAATTTCCAGCCTTGTTCTCT
5461 -----+-----+-----+-----+-----+-----+ 5520

|
AATGTAACTGATATTTAATTTCCAGGGAATGCTCCTGACAATTCGAGACTTTGCCAAAC
5521 -----+-----+-----+-----+-----+-----+ 5580
G M L L T I R D F A K H
290 300

ACGAATCACACGGAGATTCTGCGATACTCGTGATTCTATCACACGGAGAAGAGAATGTGA
5581 -----+-----+-----+-----+-----+-----+ 5640
E S H G D S A I L V I L S H G E E N V I
310 320

TTATTGGAGTTGATGATATACCGATTAGTACACACGAGATATATGATCTTCTCAACGCGG
5641 -----+-----+-----+-----+-----+-----+ 5700
I G V D D I P I S T H E I Y D L L N A A
330 340

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FIG. 4G

A (n2433)
| | Intron 5
CAAAATGCTCCCCGTCTGGCGAATAAGCCGAAAATCGTTTTTGTGCAGGCTTGTTCGAGGCG
5701 -----+-----+-----+-----+-----+-----+-----+ 5760
N A P R L A N K P K I V F V Q A C R G E
350 360
|
GTTTCGTTTTTTATTTTAATTTTAATATAAATATTTTAAATAAAATTCATTTTCAGAACGTC
5761 -----+-----+-----+-----+-----+-----+-----+ 5820
R R
GTGACAATGGATTCCCAGTCTTGGATTCTGTGCACGGAGTTCCTGCATTTCTTCGTCGTG
5821 -----+-----+-----+-----+-----+-----+-----+ 5880
D N G F P V L D S V D G V P A F L R R G
370 380
T (n1165)
|
GATGGGACAATCGAGACGGGCCATTGTTCAATTTTCTTGGATGTGTGCGGCCGCAAGTTC
5881 -----+-----+-----+-----+-----+-----+-----+ 5940
W D N R D G P L F N F L G C V R P Q V Q
390 400
| Intron 6
AGGTTGCAATTTAATTTCTTGAATGAGAATATTCCTTCAAAAAATCTAAAAATAGATTTTT
5941 -----+-----+-----+-----+-----+-----+-----+ 6000
ATTCCAGAAAGTCCCGATCGAAAAATTGCGATATAATTACGAAATTGTGATAAAATGAC
6001 -----+-----+-----+-----+-----+-----+-----+ 6060
Repeat 4

AAACCAATCAGCATCGTCGATCTCCGCCACTTCATCGGATTGGTTTGAAAAGTGGGCGGA
6061 -----+-----+-----+-----+-----+-----+-----+ 6120
----->-----
GTGAATTGCTGATTGGTCGCAGTTTTTCAGTTTAGAGGGAATTTAAAAATCGCCTTTTCGA
6121 -----+-----+-----+-----+-----+-----+-----+ 6180
AAATTAAAAATTGATTTTTTTCAATTTTTTCGAAAAATATTCGATTATTTTATATTCCTT
6181 -----+-----+-----+-----+-----+-----+-----+ 6240
A (n717)
|
GGAGCGAAAGCCCCGTCTGTAAACATTTTTTAAATGATAATTAATAAATTTTGCAGCAA
6241 -----+-----+-----+-----+-----+-----+-----+ 6300
Q
T (n1949)
|
GTGTGGAGAAAGAAGCCGAGCCAAGCTGACATTCTGATTGATAACGCAACGACAGCTCAA
6301 -----+-----+-----+-----+-----+-----+-----+ 6360
V W R K K P S Q A D I L I R Y A T T A Q
410 420

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FIG. 4H

A (n1286)

TATGTTTCGTGGAGAAACAGTGCTCGTGGATCATGGTTCATTCAAGCCGTCTGTGAAGTG
6361 -----+-----+-----+-----+-----+ 6420
Y V S W R N S A R G S W F I Q A V C E V
430 440

T (n1129, n1164)

TTCTCGACACACGCAAAGGATATGGATGTTGTTGAGCTGCTGACTGAAAGTCAATAAGAAG
6421 -----+-----+-----+-----+-----+ 6480
F S T H A K D M D V V E L L T E V N K K
450 460

T (n2430)

A (n2426)

GTCGCTTGTGGATTTTCAGACATCACAGGGATCGAATATTTTGAAACAGATGCCAGAGGTA
6481 -----+-----+-----+-----+-----+ 6540
V A C G F Q T S Q G S N I L K Q M P E
470 480
Intron 7

Repeat 5

CTTGAAACAAACAATGCATGTCTAACTTTTAAGGACACAGAAAAATAGGCAGAGGCTCCT
6541 -----+-----+-----+-----+-----+ 6600
----->
TTTGCAAGCCTGCCGCGCGTCAACCTAGAATTTTAGTTTTCTAGCTAAAATGATTGATTTT
6601 -----+-----+-----+-----+-----+ 6660
GAATATTTTATGCTAATTTTTTTGCGTTAAATTTTGAAATAGTCACTATTTATCGGGTTT
6661 -----+-----+-----+-----+-----+ 6720
CCAGTAAAAAATGTTTATTAGCCATTGGATTTTACTGAAAAACGAAAAATTTGTAGTTTTTT
6721 -----+-----+-----+-----+-----+ 6780
AACGAAATTTATCGATTTTTTAAATGTAAAAAATAAGCGAAAAATTACATCAACCATCAA
6781 -----+-----+-----+-----+-----+ 6840
GCATTTAAGCCAAAATTGTAACTCATTTAAAAATTAATTCAAAGTTGTCCACGAGTATT
6841 -----+-----+-----+-----+-----+ 6900

Repeat 5

ACACGGTTGGCGCGCGCAAGTTTGCAAAACGACGCTCCGCCTCTTTTCTGTGCGGCTT
6901 -----+-----+-----+-----+-----+ 6960

T (n1163)

GAAAACAAGGGATCGGTTTAGATTTTTTCCCAAAATTTAAATTAAATTCAGATGACATC
6961 -----+-----+-----+-----+-----+ 7020
M T S

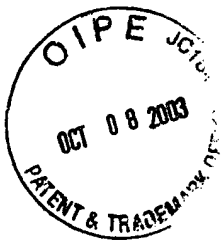
CCGCCTGCTCAAAAAGTTCTACTTTTGGCCGGAAGCACGAAACTCTGCCGTCTAAAATTC
7021 -----+-----+-----+-----+-----+ 7080
R L L K K F Y F W P E A R N S A V *
490 500



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FIG. 4I

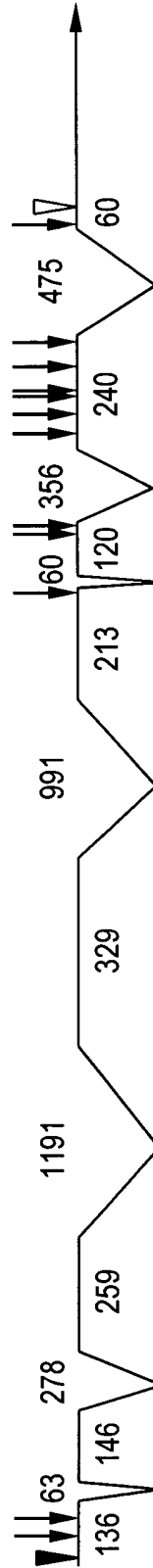
```
ACTCGTGATTCATTGCCCAATTGATAATTGTCTGTATCTTCTCCCCCAGTTCTCTTTCGC
7081 -----+-----+-----+-----+-----+-----+ 7140
CCAATTAGTTTAAAACCATGTGTATATTGTTATCCTATACTCATTTCACTTTATCATTCT
7141 -----+-----+-----+-----+-----+-----+ 7200
ATCATTTCTCTTCCCATTTTACACATTTCCATTTCTCTACGATAATCTAAAATTATGAC
7201 -----+-----+-----+-----+-----+-----+ 7260
GTTTGTGTCTCGAACGCATAATAATTTTAATAACTCGTTTTGAATTTGATTAGTTGTTGT
7261 -----+-----+-----+-----+-----+-----+ 7320
GCCCAGTATATATGTATGTACTATGCTTCTATCAACAAAATAGTTTCATAGATCATCACC
7321 -----+-----+-----+-----+-----+-----+ 7380
CCAACCCACCAACCTACCGTACCATATTCATTTTGGCCGGAATCAATTCGATTAATT
7381 -----+-----+-----+-----+-----+-----+ 7440
TTAACCTATTTTTTCGCCACAAAAATCTAATATTTGAATTAACGAATAGCATTCCCATC
7441 -----+-----+-----+-----+-----+-----+ 7500
TCTCCCGTGCCGGAATGCCTCCCGGCCTTTTAAAGTTCGGAACATTTGGCAATTATGTAT
7501 -----+-----+-----+-----+-----+-----+ 7560
AAATTTGTAGGTCCCCCCCATCATTTCCCGCCCATCATCTCAAATTGCATTCTTTTTTCG
7561 -----+-----+-----+-----+-----+-----+ 7620
CCGTGATATCCCGATTCTGGTCAGCAAAGATCT
7621 -----+-----+-----+-----+-----+ 7653
```

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FIG. 5A

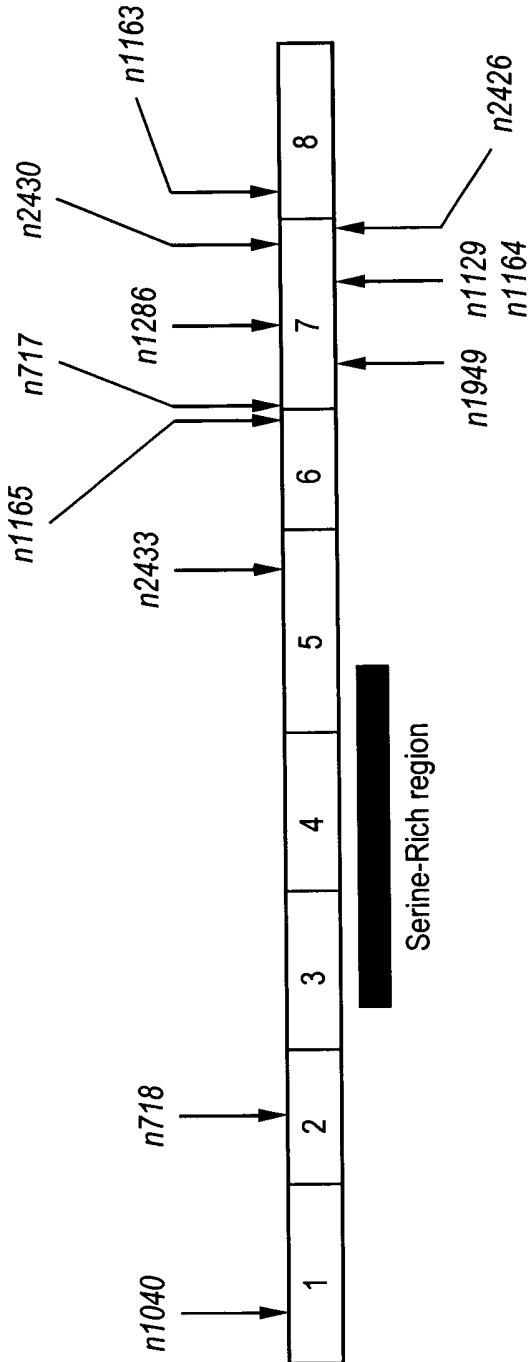
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FIG. 5B

ced-3 Mutations are Clustered

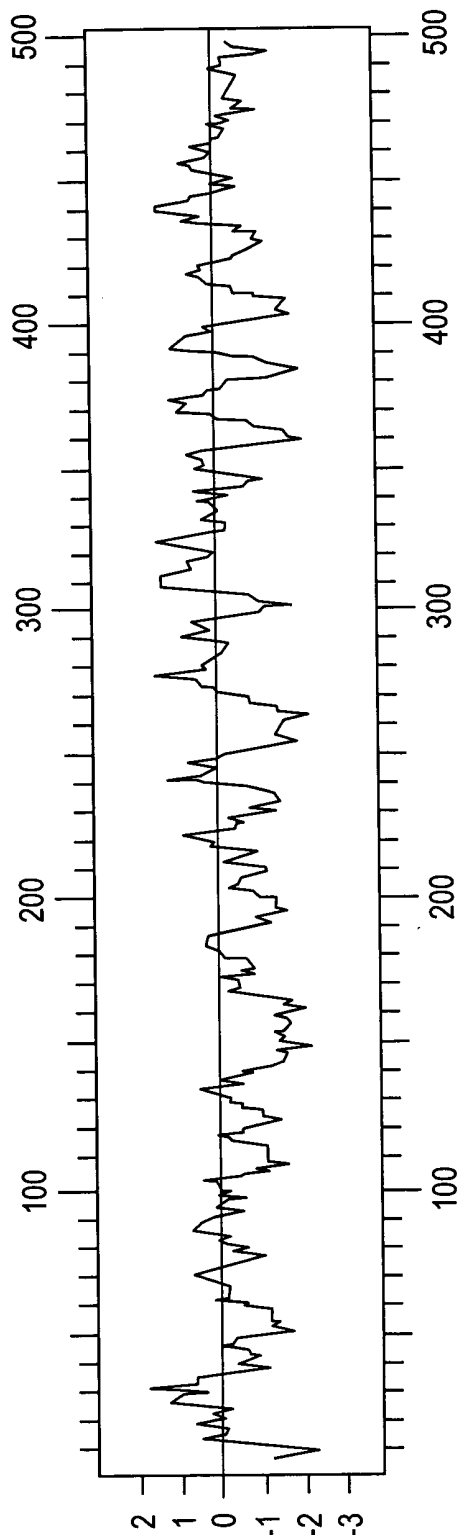




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FIG. 6





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FIG. 7

Lines
1 01 MMRQDRRSLLERNIMMFSSHLKVDEILEVLIQVLNSDNGDMINSCGTV 50
2W.....LE...K.QA.L..D.....V....R.E
3 TVS.SLI..R..... M.....

1 51 REKRREIVKAVQRPQDVAFDAFYDALRSTGHEGLAEVLEPLARSVDSNAV 100
2 .DNEK.....R..E.....D...ND..D..M..S.P .P.
3

1 101 EFECPMSPASHRRSRALSPAGYTSPTRVHRDSVSSVSFTS YQDIYSRA 149
2 PM.....S.....P .A.....I.....T...V....
3 S

1 150 RSRSR SRALHSSDRHNYSSPPVNAFPPSQSSANSSTGCSLGYSSSRN 198
2 ..S..S..P.Q.....M.AA TS.....A.....
3 T...__..P..T.....V..S..S.Q...A.....S.....T

1 199 RSFSKASGPTQYIFHEEDMNFVDAPTISRVDKTYRNFSSPRGMCLI 247
2T.AQS.....Y.....H.....L...
3 ..Y....AHS.....Y.....H.....T...L...

1 248 INNEHFQMPTRNGTKADKDNLTNLFRMGYTVICKDNLTGRGMLLTIRD 297
2I.....E..S...S
3P....IS.....I.H.....M.....

1 298 FAKHESHGDSAILVILSHGEENVIGVDDIPISTHEIYDLLNAANAPRLA 347
2 .GRNDM.....VSVNV.....
3 ...N.T.....VSVNV....X.....

1 348 NKPKIVFVQACRGERRDNGFPVLDSVDGVPFLRRGWDNRDGPLFNFLGC 397
2L.....SLI.....
3L.....V.....LI....KG...

1 398 VRPQVQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFIQAVCEVFST 447
2M..A.....L
3A.....A.....L

1 448 HAKDMDVVELLTEVNKKVACGFQTSQGSNILKQMPEMTSRLLKKFYFWPE 497
2L.....
3A.....L.....

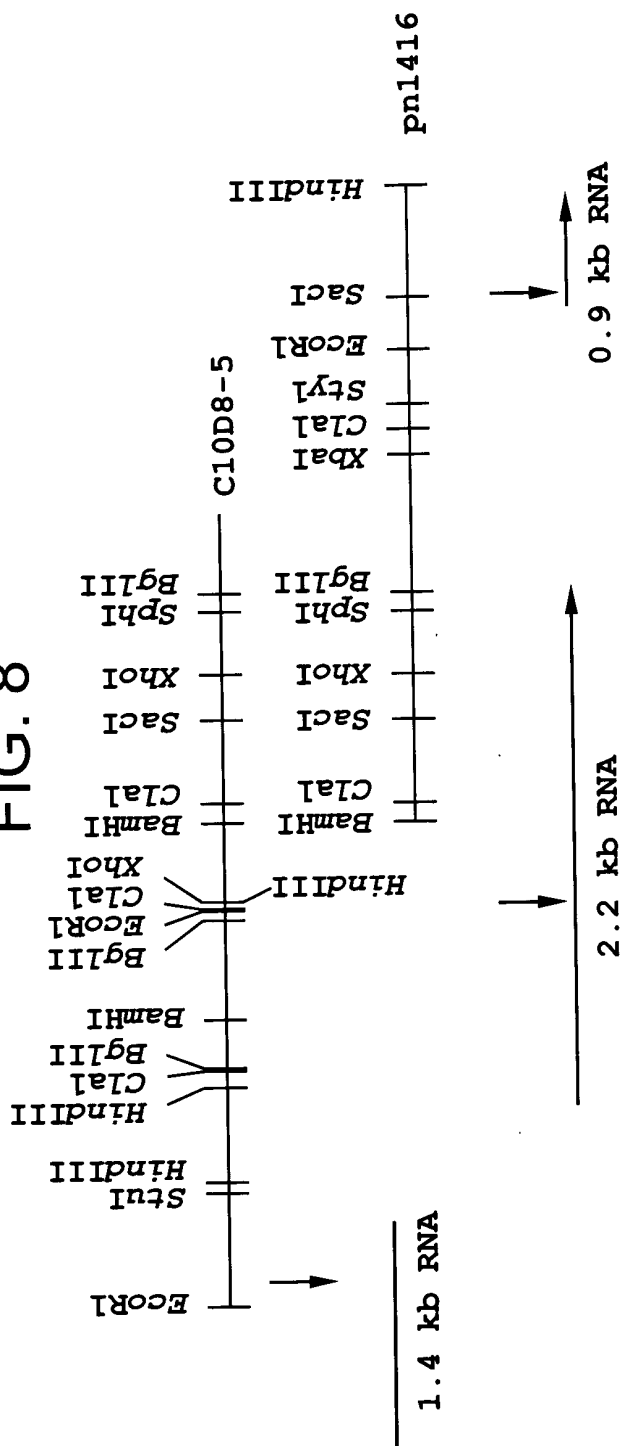
1 498 _ARN_SAV 503
2 DRG..._
3 _D..RS...

Line 1 C. elegans
Line 2 C. briggsae
Line 3 C. vulgaris

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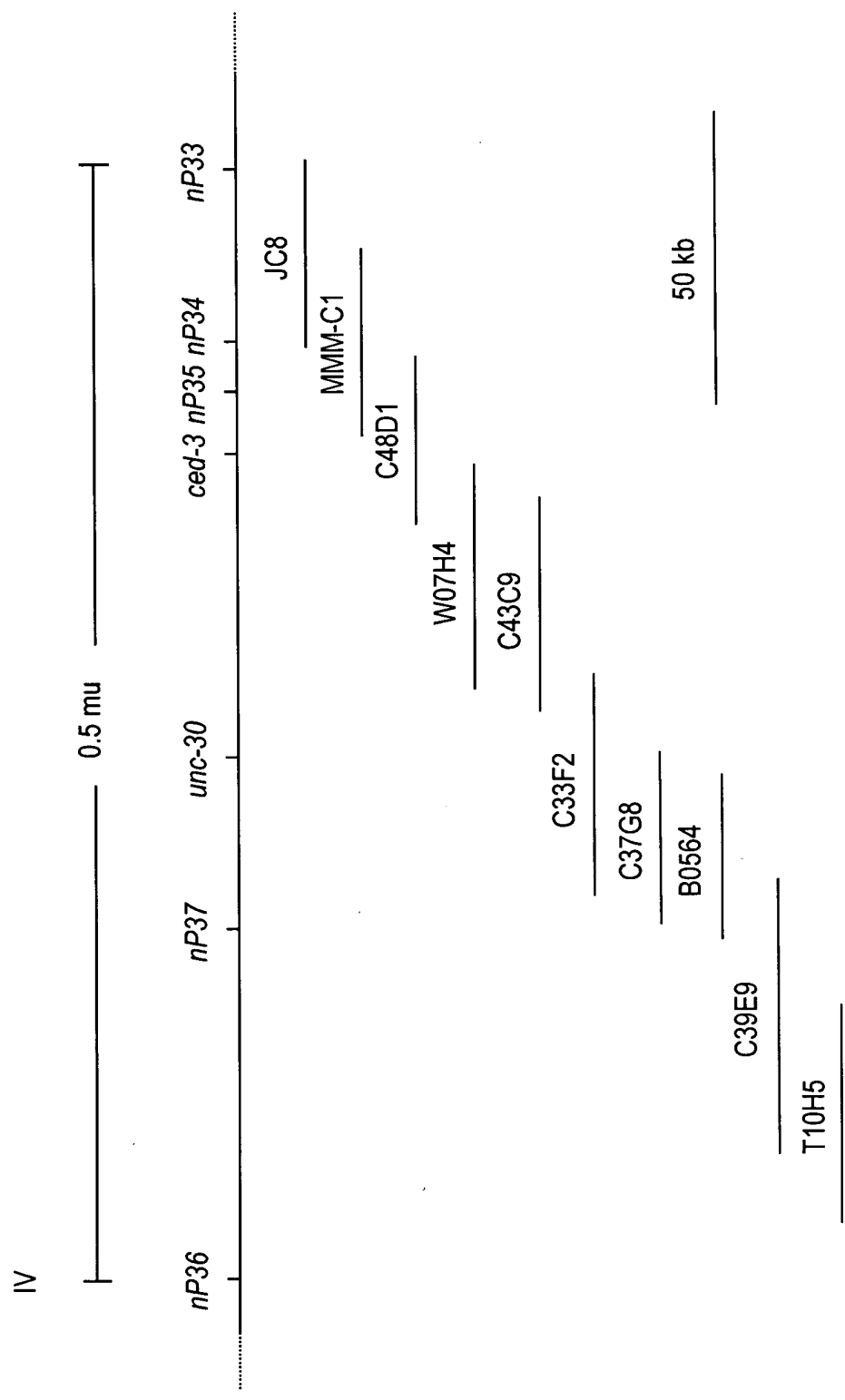
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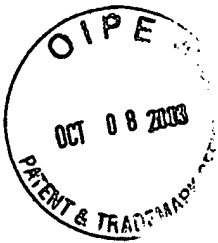
FIG. 8



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FIG. 9





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FIG. 10

Summary of the experiments to localize *ced-3* gene within C40D1

DNA	5kb			<i>ced-3</i> activity	No. lines
C48D1	BamHI	BamHI	BamHI	++	2
C48D1-20	BamHI	BglII BglII	Apal BglII BglII	++	2
C48D1-43	BamHI	BglII BglII	Apal BglII	++	1
pJ40	BamHI	BglII BglII Apal		++	1
pJ107	BamHI	BglII BglII		++	1
pJ107del28 & pJ107del34		BglII BglII		++	3
pJ107del12 & pJ107del27		BglII BglII		+	1
pJ55 & pJ56	BamHI	BglII Sall		-	12